8.2 REGULATORY REQUIREMENTS

For the assessment of similar biological products, regulatory requirements from the WHO and different regions such as the EU, the US, and the Asian Pacific Region such as Japan, Taiwan, South Korea, and China are similar and yet slightly different (Wang and Chow, 2012; Chow et al., 2013, 2015), which are briefly described below. To provide a better understanding of regulatory requirements from different regions, Table 8.1 presents a comparison of requirements for the evaluation of biosimilars.

8.2.1 The World Health Organization

As an increasingly wide range of similar biotherapeutic products (SBPs) was under development or already licensed in many countries, WHO formally recognized the need for guidance for their evaluation and overall regulation in 2007. The *Guidelines on Evaluation of Similar Biotherapeutic Products (SBPs)* were developed and adopted by the 60th meeting of the WHO Expert Committee on Biological Standardization in 2009. The intention of the guidelines was to provide globally acceptable principles for licensing biotherapeutic products claimed to be similar to the reference products that had been licensed based on a full licensing dossier (WHO, 2009). The scope of the guidelines includes well-established and well-characterized biotherapeutic products that have been marketed for a suitable period of time with proven quality, efficacy, and safety, such as recombinant DNA-derived therapeutic proteins.

8.2.1.1 Key Principles and Basic Concept

As indicated in the WHO guidelines, one of the most important principles of developing an SBP is the stepwise approach, starting with the characterization of quality attributes of the product and followed by nonclinical and clinical evaluations. Manufacturers should submit a full quality dossier that includes a complete characterization of the product, a demonstration of the consistent and robust manufacture of their product, and the comparability exercise between the SBP and the reference biotherapeutic product (RBP) in the quality part, which together serve as the basis for the possible reduction in data requirements in the nonclinical and clinical development. This principle indicates that data reduction is only possible for the nonclinical and clinical parts of the development program, and significant differences between the SBP and the chosen RBP detected during the comparability exercise would result in the requirement for more extensive nonclinical and clinical data. In addition, the amount of nonclinical and clinical data considered necessary also depends on the class of products, which calls for a case-by-case approach for different classes of products.

8.2.1.2 Reference Biotherapeutic Product

The choice of the reference biotherapeutic product is another important issue covered in the WHO guidelines. Traditionally, national regulatory authorities (NRAs) have required the use of a nationally-licensed reference product for registering generic medicines, but this may not be feasible in countries lacking nationally-licensed RBPs. Thus, additional criteria may be needed to guide the acceptability of using an RBP licensed in other jurisdictions. Considering the choice of the RBP, WHO